



GAN gene

gigaxonin

Normal Function

The *GAN* gene provides instructions for making a protein called gigaxonin. Gigaxonin is part of the ubiquitin-proteasome system, which is a multi-step process that identifies and gets rid of excess or damaged proteins or structures (organelles) within cells. The ubiquitin-proteasome system tags unneeded proteins with a small protein called ubiquitin, marking them for destruction by a complex of enzymes called a proteasome. As part of this process, enzymes called E3 ubiquitin ligases recognize the specific proteins to be broken down and attach ubiquitin to them. Gigaxonin belongs to a group of E3 ubiquitin ligases called the Cul3-E3 ligases. It helps break down protein structures called intermediate filaments, which form networks that provide support and strength to cells.

In nerve cells (neurons), gigaxonin is thought to help break down specialized intermediate filaments called neurofilaments. Neurofilaments comprise the structural framework that establishes the size and shape of nerve cell extensions called axons, which are essential for transmission of nerve impulses.

Health Conditions Related to Genetic Changes

giant axonal neuropathy

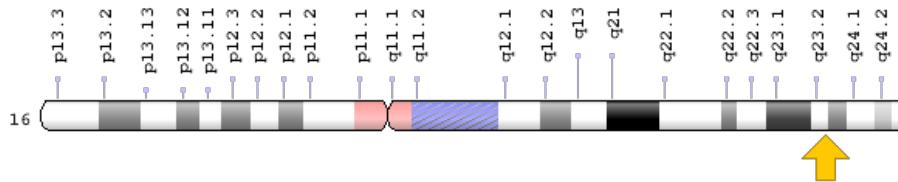
At least 47 mutations in the *GAN* gene have been identified in people with giant axonal neuropathy, an inherited disorder that causes gradually worsening loss of movement and sensation. Giant axonal neuropathy is characterized by abnormally large (giant) and deteriorating axons.

GAN gene mutations result in an unstable gigaxonin protein that breaks down easily, resulting in much less gigaxonin in cells than normal. In neurons, the reduction in gigaxonin leads to accumulation of neurofilaments that should have been destroyed by the ubiquitin-proteasome system. The neurofilaments become densely packed in the giant axons of people with giant axonal neuropathy. The giant axons are commonly seen in the peripheral nerves, which carry signals between the brain and spinal cord (central nervous system) and other areas of the body. However, axons in the central nervous system can be affected as well. These abnormal axons do not transmit signals properly and eventually deteriorate, causing severe problems in the peripheral nerves and the central nervous system.

Chromosomal Location

Cytogenetic Location: 16q23.2, which is the long (q) arm of chromosome 16 at position 23.2

Molecular Location: base pairs 81,314,941 to 81,380,198 on chromosome 16 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- GAN1
- GAN_HUMAN
- giant axonal neuropathy (gigaxonin)
- KLHL16

Additional Information & Resources

Educational Resources

- The Cell: A Molecular Approach (second edition, 2000): The Ubiquitin-Proteasome Pathway
<https://www.ncbi.nlm.nih.gov/books/NBK9957/#A1233>

GeneReviews

- Giant Axonal Neuropathy
<https://www.ncbi.nlm.nih.gov/books/NBK1136>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28GAN%5BTIAB%5D%29+OR+%28giant+axonal+neuropathy%5BTIAB%5D%29%29+OR+%28GAN1%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

OMIM

- GIGAXONIN
<http://omim.org/entry/605379>

Research Resources

- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=GAN%5Bgene%5D>
- HGNC Gene Family: BTB domain containing
<http://www.genenames.org/cgi-bin/genefamilies/set/861>
- HGNC Gene Family: Kelch like
<http://www.genenames.org/cgi-bin/genefamilies/set/617>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=4137
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/8139>
- UniProt
<http://www.uniprot.org/uniprot/Q9H2C0>

Sources for This Summary

- Allen E, Ding J, Wang W, Pramanik S, Chou J, Yau V, Yang Y. Gigaxonin-controlled degradation of MAP1B light chain is critical to neuronal survival. *Nature*. 2005 Nov 10;438(7065):224-8. Epub 2005 Oct 16.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16227972>
- Boizot A, Talmat-Amar Y, Morrogh D, Kuntz NL, Halbert C, Chabrol B, Houlden H, Stojkovic T, Schulman BA, Rautenstrauss B, Bomont P. The instability of the BTB-KELCH protein Gigaxonin causes Giant Axonal Neuropathy and constitutes a new penetrant and specific diagnostic test. *Acta Neuropathol Commun*. 2014 Apr 24;2:47. doi: 10.1186/2051-5960-2-47.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/24758703>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4234992/>
- Bomont P, Cavalier L, Blondeau F, Ben Hamida C, Belal S, Tazir M, Demir E, Topaloglu H, Korinthenberg R, Tüysüz B, Landrieu P, Hentati F, Koenig M. The gene encoding gigaxonin, a new member of the cytoskeletal BTB/kelch repeat family, is mutated in giant axonal neuropathy. *Nat Genet*. 2000 Nov;26(3):370-4.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/11062483>
- Bomont P, loos C, Yalcinkaya C, Korinthenberg R, Vallat JM, Assami S, Munnich A, Chabrol B, Kurlemann G, Tazir M, Koenig M. Identification of seven novel mutations in the GAN gene. *Hum Mutat*. 2003 Apr;21(4):446.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12655563>
- OMIM: GIGAXONIN
<http://omim.org/entry/605379>

- GeneReview: Giant Axonal Neuropathy
<https://www.ncbi.nlm.nih.gov/books/NBK1136>
- Hentati F, Hentati E, Amouri R. Giant axonal neuropathy. *Handb Clin Neurol.* 2013;115:933-8. doi: 10.1016/B978-0-444-52902-2.00052-7. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/23931822>
- Incecik F, Herguner OM, Ceylaner S, Zorludemir S, Altunbasak S. Giant axonal disease: Report of eight cases. *Brain Dev.* 2015 Sep;37(8):803-7. doi: 10.1016/j.braindev.2014.12.002. Epub 2014 Dec 19.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/25533284>
- Johnson-Kerner BL, Garcia Diaz A, Ekins S, Wichterle H. Kelch Domain of Gigaxonin Interacts with Intermediate Filament Proteins Affected in Giant Axonal Neuropathy. *PLoS One.* 2015 Oct 13; 10(10):e0140157. doi: 10.1371/journal.pone.0140157. eCollection 2015.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/26460568>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4604155/>
- Johnson-Kerner BL, Roth L, Greene JP, Wichterle H, Sproule DM. Giant axonal neuropathy: An updated perspective on its pathology and pathogenesis. *Muscle Nerve.* 2014 Oct;50(4):467-76. doi: 10.1002/mus.24321. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/24947478>
- Mahammad S, Murthy SN, Didonna A, Grin B, Israeli E, Perrot R, Bomont P, Julien JP, Kuczmarski E, Opal P, Goldman RD. Giant axonal neuropathy-associated gigaxonin mutations impair intermediate filament protein degradation. *J Clin Invest.* 2013 May;123(5):1964-75. doi: 10.1172/JCI66387. Epub 2013 Apr 15.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/23585478>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3635735/>

Reprinted from Genetics Home Reference:

<https://ghr.nlm.nih.gov/gene/GAN>

Reviewed: August 2016

Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services